DATA EVALUATION RECORD

MRID# & TITLE OF STUDY: MRID # 435348-03, *Paecilomyces fumosoroseus* Apopka Strain 97: An Avian Oral Pathogenicity and Toxicity Study in the Northern Bobwhite, FIFRA Guideline 154-16.

REVIEWED BY:

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DB BARCODE: D216262 **CASE:** 040866
REG./FILE#: 011688-RA **CHEMICAL/BIOL#:** 011688

REVIEW CONCLUSION: Supplemental. The study as reported is considered supplemental because of substantial deviations from the recommended protocols of 40 CFR 160.105 and 40 CFR 160.113 (d). Absence of dosage verification as a determination of viability concurrent with testing, and the admission of nominal dosing in preparation of stock testing solutions are of concern. Therefore, the toxicity, infectivity and pathogenicity are uncertain under reported conditions of this test. Under conditions of the test, the no observed effect dosage of *P. fumosoroseus* Apopka Strain 97 was determined as approximately 2500 mg/kg, the highest dosage tested (equivalent to maximum hazard dose of approximately 5 x 10^9 cfu/kg of body weight per day for five days), indicating *P. fumosoroseus* Apopka Strain 97 as practically nontoxic to northern bobwhite, under conditions of the test.

Additional testing for adverse effects of *P. fumosoroseus* Apopka Strain 97 to freshwater organisms may help evaluate possible toxin production.

RECOMMENDATIONS: No further avian testing is required because the fungus is not reported to grow at typical bird body temperatures and no avian incidents have been reported.

ADEQUACY OF STUDY: Supplemental/Repairable. The study may be upgraded to Core/Adequate, if W.R. Grace reprepare treatments and do assays on duplicate samples and submit surrogate data.

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MATERIALS & METHODS: The test methods were based on procedures in Series 72 of Pesticide Assessment Guidelines, Subdivision M Section 154A-16. The study was conducted in accordance with the approved Protocol with no apparent modifications. Of concern is the apparent absence of dosage verification as a determination of viability concurrent with testing, and the admission of nominal dosing in preparation of stock testing solutions. Therefore, the toxicity, infectivity and pathogenicity are uncertain under reported conditions of this test. Appropriate testing for possible toxin production was absent from the study.

The objective of the study was to determine the acute toxicity and pathogenicity of *P. fumosoroseus* Apopka Strain 97 when administered to northern bobwhite (*C. virginianus*) by oral gavage daily for five days.

The test substance was described as light brown granules and "identified per label as PFR-97®, 20% WDG BIOLOGICAL MICROBIAL INSECTICIDE FOR EXPERIMENTAL USE ONLY; ACTIVE INGREDIENT: Paecilomyces Fumosoroseus Apopka Strain 97 20%; INERT INGREDIENTS 80%."

All apparently healthy northern bobwhite (*Colinus virginianus*) were from the same hatch, pen-reared and phenotypically indistinguishable from wild birds. The birds used in this study were immature and could not be differentiated by sex. Each replicate contained five birds. There were 6 treatment replicates (a total of 30 birds were given oral dosages of 2500 mg/kg (equivalent to the maximum hazardous dose of 5×10^9 cfu/ml). The resultant total dosage was approximately 2.5×10^{10} cfu/kg of body weight over the 5-day dosing period.

The control groups consisted of a negative control and attenuated control, each group consisted of ten birds in two pens. The nominal dosage for the attenuated control was identical to the treatment group except that the test substance was inactivated by autoclaving for 20 min at 121 °C. Birds in the negative control group were administered deionized water at a dose of 1.0% (v/w) of body weight for the same five-day treatment period.

The birds were housed by treatment group during the test period. During acclimation and the test, birds were housed indoors in brooding pens which measured approximately 72 X 90 X 23 cm. External walls and ceilings were constructed of galvanized wire mesh and galvanized sheeting. Floors were constructed of galvanized wire mesh. Average ambient room temperature was 25.8 °C ± 1.0 °C with an average relative humidity of 69 % ± 10%. The photoperiod was 16 hours of light per day; birds were exposed to an average of approximately 467 lux of illumination. There was no mention of the length of the acclimation period.

Housing and husbandry practices were based on guidelines established by the National Institutes of Health. All birds were observed daily, and a record was maintained of all mortality, signs of toxicity and abnormal behavior. Individual body weights were recorded when birds were dosed on Days 0, 1, 2, 3 and 4 and on Days 11, 18, 25 and 30. Feed

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consumption was determined by measuring the change in the weight of feed presented to the birds over a given period of time. The accuracy of feed consumption values may have been affected by the unavoidable wastage of feed by birds.

REPORTED RESULTS: "No treatment related mortalities occurred during the course of the study in any of the control or treatment groups."

"There was no evidence of pathogenicity or treatment related effects in either the treatment or attenuated control groups."

DISCUSSION: Of concern is that toxicity, infectivity and pathogenicity are uncertain under reported conditions of this test. The uncertainties of toxicity, infectivity and pathogenicity result from the absence of dosage verification as based on determination of viability concurrent with testing; and the admission of nominal dosing in preparation of stock testing solutions. This is not in accord with 40 CFR Parts 160.105 and 160.113, Good Laboratory Practice Standards.

Appropriate testing for possible toxin production was absent from the study. Although this control is typically recommended in standard procedures, it is considered a supplemental "check" for this particular study for *P. fumosoroseus* Apopka Strain 97. *P. fumosoroseus* as the microbial pest control agent is not expected to survive *in situ* temperatures typical of birds.

Although these are substantial deviations from recommended protocols of 40 CFR Parts 160.105 and 160.113, further avian pathogenicity and toxicity is not justified based on the results under conditions of this test; and because *P. fumosoroseus* reportedly does not survive temperatures typical of homeothermic vertebrates, based on the public literature and extensive *in vitro* testing.

The study is therefore considered supplemental, however it is repairable. It may be upgraded to Core/Adequate, if W.R. Grace reprepare treatments and do assays on duplicate samples and submit surrogate data. Under conditions of the test, the no observed effect dosage of *P. fumosoroseus* Apopka Strain 97 was determined as approximately 2500 mg/kg, the highest dosage tested per day for a five day period. This dosage is equivalent to approximately 5×10^9 cfu/kg of body weight per day for five days, indicating *P. fumosoroseus* Apopka Strain 97 as practically nontoxic to northern bobwhite, under conditions of the test.

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